

## **REMARKS**

### **Rejection of Claims 9 and 11 Under 35 U.S.C. §103(a): Schwartz/Peyrottes**

Claims 9 and 11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Schwartz et al. as evidenced by Peyrottes et al.

Applicants respectfully disagree. Claims 9 and 11 require that at least one of X1, X2, X3, or X4 is one of the specifically recited immunostimulatory moieties for each position. Schwartz does not teach or suggest this limitation, nor does Peyrottes.

The rejection maintains that Schwartz teaches that the nucleosides present in the immunostimulatory oligonucleotide may comprise a modified backbone, including methylphosphonate (page 5). It further maintains that it would have been prima facie obvious for one of ordinary skill in the art to modify the backbone of at least one X1-X4 of Schwartz to render it as a nucleoside methylphosphonate and would have had a reasonable expectation of success for doing so because the substitution of one nucleoside linkage for another is routinely practiced in the art (page 6).

This latter statement both misses and proves the point of patentability. Applicants have defined an immunostimulatory moiety as “a chemical structure at a particular position within the immunostimulatory domain or the potentiation domain that causes the immunostimulatory oligonucleotide to be more immunostimulatory than it would be in the absence of the immunostimulatory moiety.” (specification at page 13, lines 23-26). Applicants conducted structure activity relationship (SAR) studies to determine precisely which chemical groups at precisely which position within the immunostimulatory domain would achieve this result. A summary of their positive results is shown in the specification in Table 1, page 15.

In contrast to the PTO’s statement that it would have been prima facie obvious for one of ordinary skill in the art to modify the backbone of at least one X1-X4 of Schwartz to render it as a nucleoside methylphosphonate, in fact, a nucleoside methylphosphonate substitution at position X3 or X4 did act as an immunostimulatory moiety, whereas the same substitution at position X1 or X2 does not act as an immunostimulatory moiety. The chemical structures that did act as immunostimulatory moieties at positions X1 or X2 are set forth in Table 1 and claim 9, and do not include a nucleoside methylphosphonate.

This finding also goes to the lack of a reasonable expectation of success. The PTO's statement that "the substitution of one nucleoside linkage for another is routinely practiced in the art" suggests that the PTO is looking at the wrong art. That statement may be true for the antisense art, which acts through the well-known mechanism of Watson-Crick base pairing between complementary nucleic acid strands. In that case, it is known that a nucleoside methylphosphonate can participate in such base pairing. However, the mechanism of action of the immunostimulatory domain of an immunostimulatory is far less well understood. Thus, had the person of ordinary skill substituted a nucleoside methylphosphonate at position X1 or X2, as suggested by the PTO, they would have failed in achieving Applicants' result. This further supports the nonobvious and patentable nature of Applicants' claimed invention.

For these reasons, Applicants respectfully request that this rejection be withdrawn.

Rejection of Claims 9 and 11 Under 35 U.S.C. §103(a): Nguyen in view of Schwartz

Claims 9 and 11 are rejected as being obvious over Nguyen et al in view of Schwartz et al. Applicants respectfully disagree. This rejection fails for essentially the same reasons as set forth above. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In addition, the rejection relies on legal error as to the treatment of allegedly inherent properties of a compound in an obviousness rejection. The PTO acknowledges that Nguyen does not comment on the immunostimulatory activity of the oligonucleotides that it teaches (page 7). Then it points out that "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer", citing *Atlas Powder*. This is a true statement. Such a discovery does not render an old compound new (novel). However, Nguyen does not teach Applicants' claimed oligonucleotides. It is being used in combination with Schwartz to argue that Applicants' claimed oligonucleotides are obvious. The correct standard for evaluating allegedly inherent features of a prior art compound in an obviousness analysis is whether the inherency of the feature was itself known or obvious at the Applicants' filing date.

See for, example, *Kloster Speedsteel AB v. Crucible Inc.*, 793 F.2d 1565 (Fed. Cir. 1986).

Stora bases a major argument on the undisputed fact that size change uniformity is an inherent property of the alloy disclosed in the '518 patent. That argument is unpersuasive when confronted by Stora's failure to establish at trial that that inherency would have been obvious to those skilled in the art when the invention of claim 4 was made.

Inherency and obviousness are distinct concepts. *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 1555, 220 USPQ 303, 314 (Fed. Cir. 1983) (citing *In re Spormann*, 363 F.2d 444, 448, 150 USPQ 449, 452 (1966)), *cert. denied*, 469 U.S. 851, 105 S.Ct. 172, 83 L. Ed.2d 107 (1984).

See also *In re Dillon*, 919 F.2d 688 (Fed. Cir. 1990).

The board stated that it is inherent in Dillon's compositions that they would reduce particulate emissions, that Dillon "merely recited a newly discovered function inherently possessed" by the prior art. Arguments based on "inherent" properties can not stand when there is no supporting teaching in the prior art. Inherency and obviousness are distinct concepts. *In re Spormann*, 363 F.2d 444, 448, 53 CCPA 1375, 150 USPQ 449, 452 (CCPA 1966):

[T]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.

For this further reason, Applicants respectfully be withdrawn.

Rejection of Claims 9 and 11 Under 35 U.S.C. §103(a): Zhao in view of Schwartz

Claims 9 and 11 are rejected as being obvious over Zhao et al in view of Schwartz et al. Applicants respectfully disagree. This rejection fails for essentially the same reasons cited above. Zhao does nothing to remedy this. For these reasons, Applicants respectfully request that this rejection be withdrawn.

Rejection of Claims 9-11 Under 35 U.S.C. §103(a): Agrawal in view of Schwartz

Claims 9 and 11 are rejected as being obvious over Agrawal et al in view of Schwartz et al. Applicants respectfully disagree. This rejection fails for essentially the same reasons cited above. Agrawal does nothing to remedy this. For these reasons, Applicants respectfully request that this rejection be withdrawn.

**CONCLUSION**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner believes that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned attorney at 781-933-6630.

Respectfully submitted,

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